CLAIMS

1. A method for preparing a tablet for the vaginal administration of progesterone for systemic use, comprising the steps of:

slowly mixing water with micronized progesterone, the total amount of water mixed with said micronized progesterone not exceeding the maximum wetting capacity of the amount of micronized progesterone, whereby to obtain wetted micronized progesterone;

drying said wetted micronized progesterone to a humidity content of substantially 0%, whereby to form substantially dry micronized progesterone;

mixing said substantially dry micronized progesterone with other pharmaceutically acceptable excipients or diluents therefor; and

forming a tablet by direct compaction of said substantially dry micronized progesterone which has been mixed with said other pharmaceutically acceptable excipients or diluents therefor.

2. A method according to claim 1 for preparing a tablet for the vaginal administration of progesterone for systemic use, comprising the steps of:

slowly mixing water with micronized progesterone, the total amount of water mixed with said micronized progesterone not exceeding the maximum wetting capacity of the amount of micronized progesterone, whereby to obtain wetted micronized progesterone;

drying said wetted micronized progesterone to a humidity content of substantially 0%, whereby to form substantially dry micronized progesterone;

mixing said substantially dry micronized progesterone with other pharmaceutically acceptable excipients or diluents therefor, including an effervescent; and

forming a tablet by direct compaction of said substantially dry micronized progesterone which has been mixed with said other pharmaceutically acceptable excipients or diluents therefor, including said effervescent.

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3. A method according to claim 2 for preparing a tablet for the vaginal administration of progesterone for systemic use, comprising the steps of:

slowly mixing water with micronized progesterone, the total amount of water mixed with said micronized progesterone does not exceed the maximum wetting capacity of the amount of micronized progesterone, whereby to obtain wetted micronized progesterone;

drying said wetted micronized progesterone to a humidity content of substantially 0%, whereby to form substantially dry micronized progesterone;

sieving a first lubricant to obtain a sieved first lubricant;

mixing said substantially dry micronized progesterone with said sieved first lubricant and a material selected from a first filler or a disintegrant to form a first mixture;

mixing a binder which binds dry particles with said first mixture to form a second mixture;

intimately mixing an effervescent and a first quantity of a second filler to form a third mixture;

sieving said third mixture to obtain a sieved third mixture, and then intimately mixing said sieved third mixture and said second mixture to form a fourth mixture;

intimately mixing said fourth mixture with a second quantity of said second filler to form a fifth mixture;

sieving a second lubricant and a material selected from a saponificant or a third lubricant to obtain, respectively, sieved second lubricant and sieved third lubricant;

intimately mixing said sieved second lubricant and said sieved third lubricant with said fifth mixture to form a sixth mixture; and

tabletting said sixth mixture by direction compaction to form a tablet.

4. A method according to claim 3, wherein said first lubricant is sieved through sieves having a pore size of between about 400 and 450 microns.

5. A method according to claim 4, wherein said first lubricant is sieved through sieves having a pore size of about 425 microns.

6. A method according to any of claims 3 to 5, wherein said third mixture is sieved through sieves having a pore size of between about 400 and 450 microns

7. A method according to claim 6, where said pore size is about 425 microns.

8. A method according to any of claims 3 to 7 wherein said sieved second lubricant and said sieved third lubricant are sieved through sieves having a pore size of between about 100 and 150 microns.

9. A method according to claim 8, wherein said pore size is about 125 microns.

10. A method according to any of claims 3 to 9, wherein said first lubricant is silicon dioxide (colloidal anhydrous silica).

11. A method according to any of claims 3 to 10, wherein said material selected from a first filler or a disintegrant is a starch exhibiting good flow properties.

12. A method according to claim 11 wherein said starch is derived from corn (maize), potatoes or wheat.

13. A method according to claim 12 wherein said starch is cornstarch 1500.

14. A method according to any of claims 3 to 13, wherein said binder which binds dry particles is polyvinylpyrrolidone (povidone).

15. A method according to claim 14, wherein said binder which binds dry particles is Povidone 30.

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16. A method according to any of claims 3 to 15, wherein said second filler is derived from a natural source.

17. A method according to claim 16, wherein said second filler is selected from lactose or a composition composed principally of lactose.

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18. A method according to any of claims 3 to 17, wherein said first portion and said second portion of said second filler are of generally the same size.

19. A method according to any of claims 3 to 18, wherein said effervescent is prepared prior to said intimate mixing of said first portion of said second filler with said effervescent.

20. A method according to any of claims 3 to 18, wherein said effervescent is prepared *in situ* as part of said intimate mixing of said first portion of said second filler with said effervescent.

21. A method according to any of claims 3 to 20, wherein said intimate mixing of said first portion of said second filler with said effervescent comprises non-intimately mixing said first portion of said second filler with said effervescent and passing the resultant non-intimately mixed mixture through a sieve having an average pore size between about 400 and 450 microns, to obtain said third mixture.

22. A method according to claim 21, wherein said intimate mixing of said first portion of said second filler with said effervescent comprises non-intimately mixing said first portion of said second filler with said effervescent and passing the resultant non-intimately mixed mixture through a sieve having an average pore size of about 425 microns diameter to obtain said third mixture.

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23. A method according to any of claims 3 to 22, wherein said intimate mixing of said second mixture with said third mixture to obtain said fourth mixture is

accomplished by non-intimately mixing said second mixture with said third mixture to obtain a non-intimately mixed mixture and sifting said non-intimately mixed mixture through a sieve having an average pore size between about 400 and 450 microns to obtain said fourth mixture.

24. A method according to claim 23, wherein said intimate mixing of said second mixture with said third mixture to obtain said fourth mixture is accomplished by non-intimately mixing said second mixture with said third mixture to obtain a non-intimately mixed mixture and sifting said non-intimately mixed mixture through a sieve having an average pore size of about 425 microns diameter to obtain said fourth mixture.

25. A method according to any of claims 3 to 24, wherein said second lubricant is selected from magnesium stearate, talc, sodium lauryl sulfate, and phosphates known in the art to function as lubricants.

26. A method according to claim 25, wherein said lubricant is magnesium stearate.

27. A method according to any of claims 3 to 26, wherein said material selected from a saponificant or a third lubricant is sodium lauryl sulfate.

28. A method according to any of claims 2 to 27, wherein said effervescent is a mixture of a pharmaceutically acceptable carboxylic or dicarboxylic acid and a pharmaceutically acceptable salt of HCO_3^-.

29. A method according to claim 28, wherein said pharmaceutically acceptable carboxylic or dicarboxylic acid is selected from adipic acid or tartaric acid.

30. A method according to claim 28 or 29, wherein said pharmaceutically acceptable salt of HCO_3^- is as sodium bicarbonate.

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31. A method according to any of claims 28 to 30, wherein said pharmaceutically acceptable carboxylic or dicarboxylic acid and said bicarbonate are present in an amount providing a molar excess of -COOH groups.

32. A method according to any of claims 28 to 31, wherein said effervescent comprises a mixture of adipic acid and sodium bicarbonate.

33. A method according to any of claims 2-32, wherein said effervescent comprises between about 6 and 10 wt.%, preferably about 8 wt.% of the tablet.

34. A method according to any of claims 1 to 33 wherein the amount of water mixed with said micronized progesterone is between about 25 and 28 wt.% of the amount of micronized progesterone.

35. A method according to claim 34, wherein the amount of water mixed with said micronized progesterone is about 28 wt.% of the amount of micronized progesterone.

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36. A method according to any of claims 1 to 35, wherein said water is added to said micronized progesterone at rate of between about 6 to 9 ml per minute.

37. A method according to any of claims 1 to 36, wherein said water is mixed with said micronized progesterone at a mixing speed of between about 25-33.3 rpm.

38. A method according to any of claims 1 to 37 wherein said drying of said wetted micronized progesterone is done at a temperature of between about 55°C and about 60°C.

39. A method according to any of claims 1 to 38 wherein all of said mixing steps are carried out at a temperature of between about 15°C and 30°C.

40. A tablet prepared by the steps of:

slowly mixing water with micronized progesterone, the total amount of water mixed with said micronized progesterone not exceeding the maximum wetting capacity of the amount of micronized progesterone, whereby to obtain wetted micronized progesterone;

drying said wetted micronized progesterone to a humidity content of substantially 0%, whereby to form substantially dry micronized progesterone;

mixing said substantially dry micronized progesterone with other pharmaceutically acceptable excipients or diluents therefor; and

forming a tablet by direct compaction of said substantially dry micronized progesterone which has been mixed with said other pharmaceutically acceptable excipients or diluents therefor.

41. A tablet prepared by the steps of:

slowly mixing water with micronized progesterone, the total amount of water mixed with said micronized progesterone not exceeding the maximum wetting capacity of the amount of micronized progesterone, whereby to obtain wetted micronized progesterone;

drying said wetted micronized progesterone to a humidity content of substantially 0%, whereby to form substantially dry micronized progesterone;

mixing said substantially dry micronized progesterone with other pharmaceutically acceptable excipients or diluents therefor, including an effervescent; and

forming a tablet by direct compaction of said substantially dry micronized progesterone which has been mixed with said other pharmaceutically acceptable excipients or diluents therefor, including said effervescent.

42. A tablet prepared by the steps of:

slowly mixing water with micronized progesterone, the total amount of water mixed with said micronized progesterone does not exceed the maximum wetting

capacity of the amount of micronized progesterone, whereby to obtain wetted micronized progesterone;

drying said wetted micronized progesterone to a humidity content of substantially 0%, whereby to form substantially dry micronized progesterone;

sieving a first lubricant to obtain a sieved first lubricant;

mixing said substantially dry micronized progesterone with said sieved first lubricant and a material selected from a first filler or a disintegrant to form a first mixture;

mixing a binder which binds dry particles with said first mixture to form a second mixture;

intimately mixing an effervescent and a first quantity of a second filler to form a third mixture;

sieving said third mixture to obtain a sieved third mixture, and then intimately mixing said sieved third mixture and said second mixture to form a fourth mixture;

intimately mixing said fourth mixture with a second quantity of said second filler to form a fifth mixture;

sieving a second lubricant and a material selected from a saponificant or a third lubricant to obtain, respectively, sieved second lubricant and sieved third lubricant;

intimately mixing said sieved second lubricant and said sieved third lubricant with said fifth mixture to form a sixth mixture; and

tabletting said sixth mixture by direction compaction to form a tablet.

43. A tablet comprising between about 6 to 20 wt.% progesterone and between about 5 to 12 wt.% effervescent.

44. A tablet according to claim 43 comprising between about 8 to 12 wt.% progesterone.

45. A tablet according to claim 43 or 44 comprising between about 6 to 8 wt.% effervescent.